Generation of brain organoid to study tumorigenesis

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Contact person

Diana Al Delbany

Organisation

Name of the organisation Vrije Universiteit Brussel (VUB)
Department Biomedical Sciences

Specific Research Group or Service
REPRODUCTION AND GENETICS research Group (REGE)
Country Belgium
Geographical Area Brussels Region
Name of the organisation Vrije Universiteit Brussel (VUB)
Department Genetics Reproduction and development research group
Country Belgium
Geographical Area Brussels Region

SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research
Type of method	In vitro - Ex vivo
Species from which cells/tissues/organs are derived	human embryonic stem cells
Type of cells/tissues/organs	human pluripotent stem cells

DESCRIPTION

Method keywords

HUman brain organoids
tumor
human embryonic stem cell derived organoid model

Scientific area keywords

Human Stem cells
tumorigenesis
3D organoid models
hESC-derived organoids

Method description

This method uses human pluripotent stem cells (hPSCs), including embryonic and induced pluripotent stem cells, to generate cortical brain organoids and model brain tumorigenesis through targeted genetic manipulation. The aim is to create a physiologically relevant, *in vitro* 3D system that mimics early brain development and allows the study of cancer initiation and progression. Organoids are guided through neural induction and maturation using stage-specific culture conditions and matrix support, resulting in self-organized brain-like structures. Genetic alterations are introduced via lentiviral transduction of oncogenes and tumor suppressor knockouts to simulate tumor development. Fluorescent markers are used to trace cell origin and monitor growth dynamics over time. This model enables spatial and temporal investigation of tumor biology in a controlled setting and represents a promising tool for studying human brain cancer. Additionally, it has potential applications in modeling other cancers, such as liver tumors, offering an ethical alternative to animal experimentation.

Lab equipment

This method requires lab equipment including a biosafety cabinet for sterile cell culture work, an orbital shaker for organoid agitation, a fluorescent microscope for live imaging, and a flow cytometer to analyze and separate transduced cell populations. Access to lentiviral production facilities.

Method status

History of use
Internally validated
Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

- This method allows the simultaneous analysis of transformed and non-transformed tissues within the same organoid, enabling direct comparison in a controlled 3D environment.
- It supports high-throughput experimentation, as multiple organoids can be generated and analyzed in parallel.
- The approach offers a physiologically relevant model for tumor initiation and progression and reduces reliance on animal models.

Challenges

- One major limitation is the variability between organoid batches, which can affect reproducibility and data interpretation.
- The method is also labor-intensive and requires significant hands-on time, technical expertise, and access to specialized equipment and reagents.

Modifications

- Future optimization may focus on reducing batch-to-batch variability by standardizing organoid generation protocols or using automation.
- Advanced imaging techniques could enhance resolution and data richness.
- Improvements in viral transduction efficiency could be also improved.

Future & Other applications

This method has broad potential beyond brain tumor modeling. It can be adapted to generate organoids from other tissues such as liver, pancreas, or colon, to study various types of cancer or organ-specific diseases. Additionally, it holds promise for drug

screening, personalized medicine, and developmental biology studies.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

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Associated documents

Mutagensis induction in brain organoids.png

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